UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/039,642	10/24/2001	Yukio Sudo	JG-SIK-5108/500676.20005	9277

26418 7590 11/03/2003

REED SMITH, LLP
ATTN: PATENT RECORDS DEPARTMENT
599 LEXINGTON AVENUE, 29TH FLOOR
NEW YORK, NY 10022-7650

EXAMINER	
LU, FRANK WEI MIN	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 11/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/039,642	SUDO ET AL.	
	Examiner	Art Unit	
	Frank W Lu	1634	

-- The MAILING DATE of this communication appears on the cover sheet with th correspond nce addr ss --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 August 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of species of Group (1), the double stranded DNA recognizing substance is a double stranded DNA recognizing antibody (claim 4), filed on August 8, 2003 is acknowledged. Therefore, claims 1-4 and 8-11 will be examined.

Information Disclosure Statement

2. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Claim Objections

3. Claims 1-3 are objected to because of the following informality: "double stranded DNA" in preamble should be either "a double stranded DNA" or "double stranded DNAs".

4. Claim 1 is objected to because of the following informality: "double stranded DNA" in step (2) should be "the double stranded DNA" since "double stranded DNA" has appeared once in the preamble.

5. Claim 2 is objected to because of the following informalities:(1) "double stranded DNA" in steps (2) and (3) should be "the double stranded DNA" since "double stranded DNA" has

appeared once in the preamble; and (2) "an analyte" in step (2) should be "the analyte" since "an analyte" " has appeared once in the preamble.

6. Claim 3 is objected to because of the following informalities: (1) "double stranded DNA" in steps (2) and (4) should be "the double stranded DNA" since "double stranded DNA" has appeared once in the preamble; and (2) "an analyte" in step (2) should be "the analyte" since "an analyte" " has appeared once in the preamble.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 2 and 3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. Claims 2 and 3 are rejected as vague and indefinite in view of step (2) of the claims 2 and 3 because it is unclear that, if an electric field is between the support on which the double stranded DNA recognizing substance is immobilized and the analyte, how double stranded DNA present in an analyte can be directed toward the double stranded DNA recognizing substance immobilized on the support. It is known in the art that double stranded DNA present in an analyte can be directed toward the double stranded DNA recognizing substance immobilized on the support when the support and the analyte are inside the electric field. Please clarify.

10. Claims 2 and 3 are rejected as vague and indefinite in view of steps (1) and (2) of the claims. Since step (1) of the claim have contacted the analyte containing a double stranded DNA with a double stranded DNA recognizing substance immobilized on a support, it is unnecessary to require to direct the double stranded DNA present in the analyte toward the double stranded DNA recognizing substance immobilized on a support as recited in step (2) and it seems that steps (1) and (2) do not correspond each other. Please clarify.

11. Claim 8 is rejected as vague and indefinite because it is unclear whether " a reaction system" has a complex formed by the double stranded DNA and the double stranded DNA recognizing substance or not. If " a reaction system" does not have a complex formed by the double stranded DNA and the double stranded DNA recognizing substance, the insertion agent in the reaction system cannot insert into the double stranded DNA. Please clarify.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 1 and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Vinayagamoorthy *et al.*, (US Patent No. 5,912,129, published on June 15, 1999).

Vinayagamoorthy *et al.*, teach a process of amplifying a DNA by a polymerase chain reaction utilizing a polymerase enzyme. The method comprised: (a) fixing a solid medium within a container, said solid medium having a surface that bound nucleic acid; (b) binding said DNA to

said solid medium fixed within said container; (c) introducing into said container a first liquid medium and subjecting said DNA to conditions or reagents for denaturing double-stranded DNA, thereby creating single-stranded DNA; (d) removing said first liquid medium from said container resulting from step (c) and removing said conditions or reagents for denaturing double-stranded DNA; (e) introducing a second liquid medium containing said polymerase enzyme into said container resulting from step (d) and subjecting said single-stranded DNA to polymerization, thereby creating double-stranded DNA using said single-stranded DNA as a template for new strands of complementary base sequences; (f) removing said second liquid medium from said container resulting from step (e); (g) repeating steps (c)-(f) a plurality of times to amplify said DNA; and (h) removing said amplified DNA from said solid medium. The amplified DNA was detected by dot blot (see claim 16 in columns 21 and 22 and Example 1 in columns 14 and 15). Note that said solid medium was a magnetic substrate (ie., beads) coated with anti-DNA antibody (see column 6, lines 47-59).

Regarding claims 1 and 4, since Vinayagamoorthy *et al.*, teach fixing a solid medium within a container, said solid medium having a surface that binds nucleic acid wherein said solid medium is a magnetic substrate (ie., beads) coated with anti-DNA antibody, Vinayagamoorthy *et al.*, disclose contacting the analyte having a DNA with a double stranded DNA recognizing substance (ie., anti-DNA antibody) immobilized on a support as recited in step (1) of claim 1. Since Vinayagamoorthy *et al.*, teach introducing into said container a first liquid medium and subjecting said DNA to conditions or reagents for denaturing double-stranded DNA, DNA bound to said solid medium taught by Vinayagamoorthy *et al.*, is a double stranded DNA and anti-DNA antibody taught by Vinayagamoorthy *et al.*, is a double stranded DNA recognizing

antibody as recited in claims 1 and 4. Since Vinayagamoorthy *et al.*, teach that a single stranded DNA denatured from the double-stranded DNA bound to anti-DNA antibody is amplified and is detected by dot blot, Vinayagamoorthy *et al.*, discloses to indirectly qualitatively measure double stranded DNA bound to the double stranded DNA recognizing substance by detecting amplified PCR product as recited in step (2) of claim 1.

Therefore, Vinayagamoorthy *et al.*, teach all limitations recited in claims 1 and 4.

14. Claim 2 is rejected under 35 U.S.C. 102(b) as being anticipated by Bujard *et al.*, (US Patent No. 4,868,111, published on September 19, 1989).

Since claim 2 is vague and indefinite (see above rejection under 35 USC 112, second paragraph), the rejection is based on contacting the double stranded DNA present in an analyte with the double stranded DNA recognizing substance immobilized on the support by applying an electric field wherein the support and the analyte are inside the electric field and the rejection is not based on directly contacting the double stranded DNA present in an analyte with the double stranded DNA recognizing substance immobilized on the support as recited in step (1) of claim 2.

Bujard *et al.*, teach gram-positive expression control sequences. As shown in Example 1, two μg of plasmid pUB110 were digested to completion with the restriction endonuclease PvuII. An octameric KpnI linker was ligated to the PvuII ends. Following the ligation, the DNA was digested to completion with the endonucleases KpnI and EcoRI. The resulting digested DNA was electrophoresed through a 1% low melting temperature agarose gel containing 1 μg/ml

ethidium bromide. After 2 hours of electrophoresis at 70V, the DNA bands were visualized by fluorescence, and the upper 3.5 Kb band was excised from the gel (see column 12, lines 4-15).

Regarding claim 2, since Bujard *et al.*, teach that the digested DNA is electrophoresed through a 1% low melting temperature agarose gel containing 1 μg/ml ethidium bromide, the digested DNA forms complexes with ethidium bromide after it enters the gel and moves through the gel in the electric field (ie., electrophoresis). Since only double stranded DNA can be digested with endonucleases KpnI and EcoRI, the digested DNA is double stranded as recited in claim 2. Thus Bujard *et al.*, disclose to direct double stranded DNA present in an analyte toward the double stranded DNA recognizing substance immobilized on the support as recited in claim 2 wherein ethidium bromide is the double stranded DNA recognizing substance. Since Bujard *et al.*, teach that, after 2 hours of electrophoresis at 70V, the DNA bands are visualized by fluorescence, and the upper 3.5 Kb band is excised from the gel, Vinayagamoorthy *et al.*, discloses to qualitatively measure double stranded DNA bound to the double stranded DNA recognizing substance by visualizing the digested fluorescence DNA bands as recited in step (3) of claim 2.

Therefore, Bujard *et al.*, teach all limitation recited in claim 2.

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 8, 9, and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vinayagamoorthy *et al.*, (June 15, 1999) as applied to claims 1 and 4 above, and further in view of Piunno *et al.*, (Anal. Chem., 67, 2635-2643, 1995).

The teachings of Vinayagamoorthy *et al.*, have been summarized previously, *supra.* Vinayagamoorthy *et al.*, do not disclose to measure the double stranded DNA in the complex formed by the double stranded DNA present in the analyte and the double stranded DNA recognizing substance by detecting the insertion agent (ie., a DNA intercalator) inserted into the double stranded DNA using a fluorescence method as recited in claims 8, 9, and 11.

Piunno *et al.*, teach fiber-optic DNA sensor for fluorometric nucleic acid determination. After single-stranded deoxyribonucleic acid thymidylic acid icosanucleotides (dT20) on the surfaces of derivatized quartz optical fibers hybridized with their complementary ssDNA (cDNA) or ssRNA (cRNA) from solution, the hybridization on optical fibers was detected by the use of the fluorescent DNA stain ethidium bromide (EB) (see page 2635, abstract). The fluorescence intensity was directly proportional to the amount of complement DNA present in solution (see page 2636, left column, last paragraph).

Regarding claims 8, 9, and 11, since it is known that ethidium bromide inserts into a double stranded DNA and a complex formed by the double stranded DNA and the ethidium bromide (ie., a DNA intercalator) shows a fluorescence under UV light, claims 8, 9, and 11 are disclosed by Piunno *et al.*,

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have measured the double stranded DNA in the complex formed by the double stranded DNA present in the analyte and the double stranded DNA recognizing substance by detecting the insertion agent (ie., a DNA intercalator such as ethidium bromide) inserted into the double stranded DNA as recited in claims 8, 9, and 11 in view of the prior art of Vinayagamoorthy *et al.*, and Piunno *et al.*. One having ordinary skill in the art would have been motivated to do so because direct detection of a double stranded DNA by the use of the fluorescent DNA stain ethidium bromide (EB) (ie., a DNA intercalator) is much fast than the method used by Vinayagamoorthy *et al.*, (ie. PCR and dot blot), and the simple replacement of one known detection method (ie., the method taught by Vinayagamoorthy *et al.*,) from another known method (i.e., staining with ethidium bromide taught by Piunno *et al.*,) for detecting a double stranded DNA would have been, in the absence of convincing evidence to the contrary, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made since the replacement would save time and cost during the process for detecting the double stranded DNA in the analyte as recited in claim 1.

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their

expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

17. Claims 8-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vinayagamoorthy *et al.*, (June 15, 1999) as applied to claims 1 and 4 above, and further in view of Liu *et al.*, (Analytica Chimica Acat, 335, 239-243, 1996).

The teachings of Vinayagamoorthy *et al.*, have been summarized previously, *supra.* Vinayagamoorthy *et al.*, do not disclose to measure the double stranded DNA in the complex formed by the double stranded DNA present in the analyte and the double stranded DNA recognizing substance by detecting the insertion agent (ie., a DNA intercalator with an electrochemical activity) inserted into the double stranded DNA by electrochemical means as recited in claims 8-10.

18. Liu *et al.*, teach voltammetric determination of sequence-specific DNA by electroactive intercalator on graphite electrode. After a single-stranded DNA on a chemically-modified graphite electrode hybridized with its complementary DNA from a solution containing ethidium bromide (EB), the double stranded DNA/EB system was formed on the electrode surface and the anodic peak waves of the EB bound to the double-stranded DNA in cyclic voltammetry were

used for the determination of the hybridization (see abstract in page 239, right column in page 241 and Figure 1).

Regarding claims 8-10, since it is known that ethidium bromide binds with polynucleotides by intercalation into the base pair stakes of the DNA double helix structure (see page 240, left column, third paragraph), ethidium bromide is a DNA intercalator. Since Liu *et al.*, teach that binding of ethidium bromide to the double-stranded DNA is detected by cyclic voltammetry (ie., electrochemical measurements), ethidium bromide is a DNA intercalator with an electrochemical activity and claims 8-10 are disclosed by Liu *et al.*.

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have measured the double stranded DNA in the complex formed by the double stranded DNA present in the analyte and the double stranded DNA recognizing substance by detecting the insertion agent (ie., a DNA intercalator such as ethidium bromide) inserted into the double stranded DNA by electrochemical means as recited in claims 8-10 in view of the prior art of Vinayagamoorthy *et al.*, and Liu *et al.*. One having ordinary skill in the art would have been motivated to do so because the double stranded DNA/ethidium bromide electrode system taught by Liu *et al.*, represents an important approach to improve the analytical selectivity of biosensor by taking the advantage of a known biological recognition process (ie., binding of ethidium bromide to the double-stranded DNA) and has been shown to be reproducible, regenerable, and sensitive (see page 243, right column), and the simple replacement of one known detection method (ie., the method taught by Vinayagamoorthy *et al.*,) from another known method (i.e., the method taught by Liu *et al.*,) for detecting a double stranded DNA would have been, in the absence of convincing evidence to the contrary, *prima*

facie obvious to one having ordinary skill in the art at the time the invention was made since the replacement would not change the detection results.

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

Conclusion

18. No claim is allowed.

19. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is either (703) 308-4242 or (703) 305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (703) 305-1270. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Frank Lu
PSA
October 28, 2003